SUPPLEMENTAL MATERIAL

Identification of Tazarotenic Acid as the First Xenobiotic Substrate of Human Retinoic Acid Hydroxylase CYP26A1 and CYP26B1

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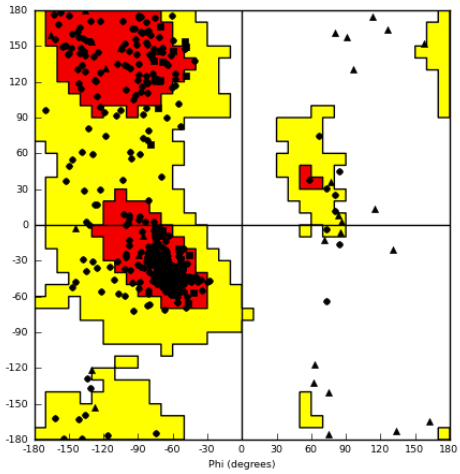
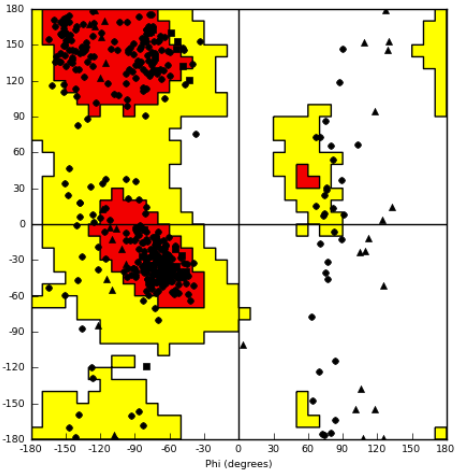
Supplemental Figure 1. CYP26A1 and CYP26B1 Ramachandran Plots. Statistical analysis Ramachandran plots is noted in Table 1.

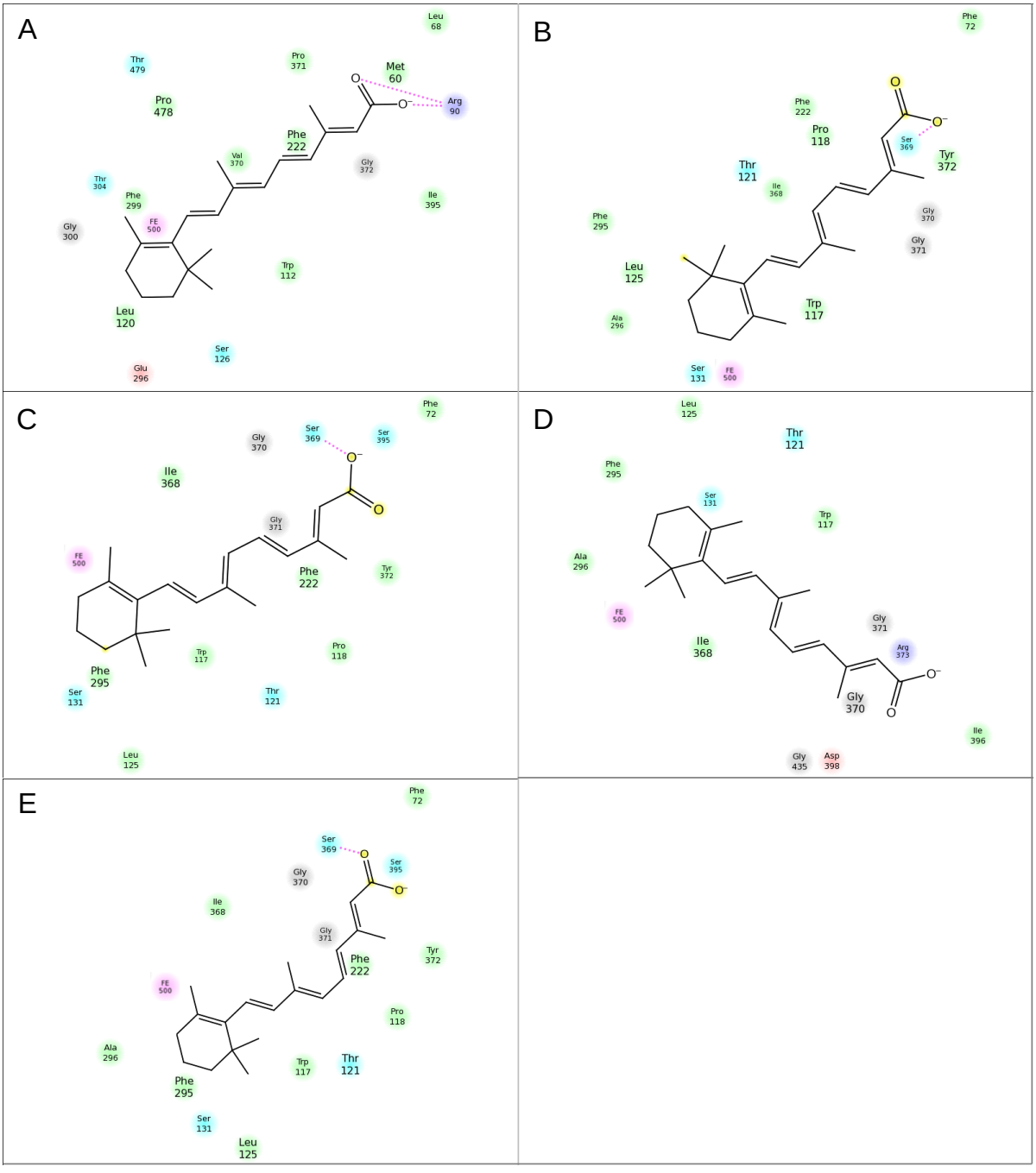
26A1 Ramachandran Plot



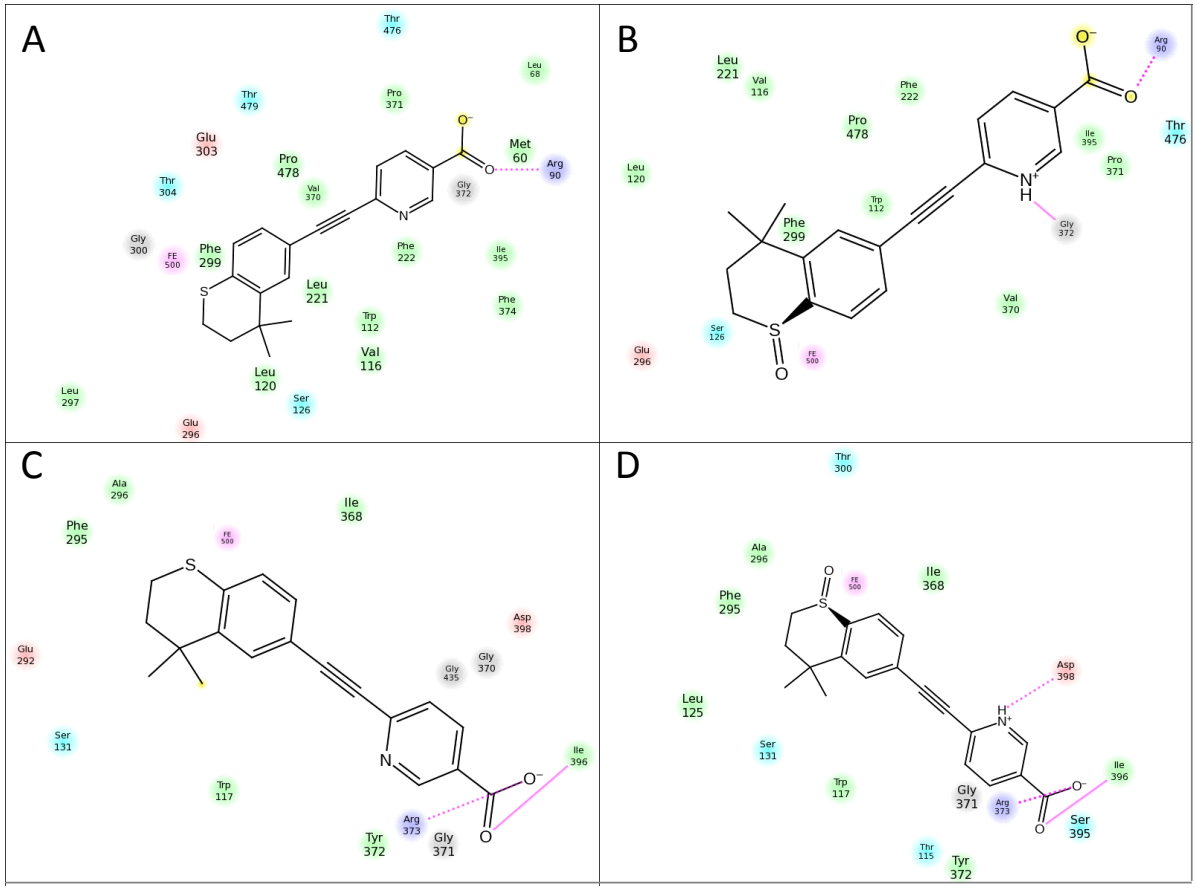
26B1 Ramachandran Plot



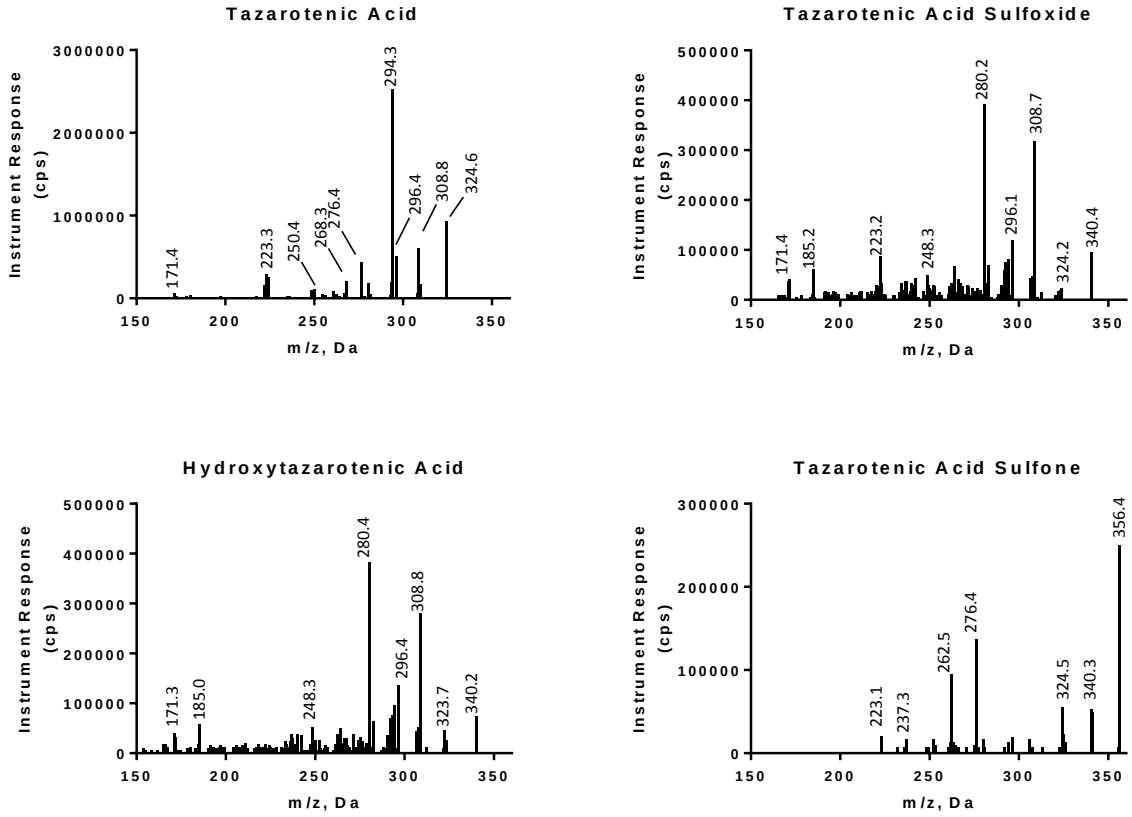
Supplemental Figure 2. Ligand interaction diagram for *at*-RA docked in the active site of CYP26A1 and CYP26B1. Analysis of the active site ligand interactions for *at*-RA docked in the active site of CYP26A1 (A) and CYP26B1 (4-(*R*)-OH, B; 4-(*S*)-OH, C; 16-OH, D; 18-OH, E) shows the hydrophobic (green), hydrophilic (blue), electrostatic (red/purple) and metal (pink) interactions located within 3.0 Å of *at*-RA. Hydrogen bonding interactions are depicted by dashed lines.



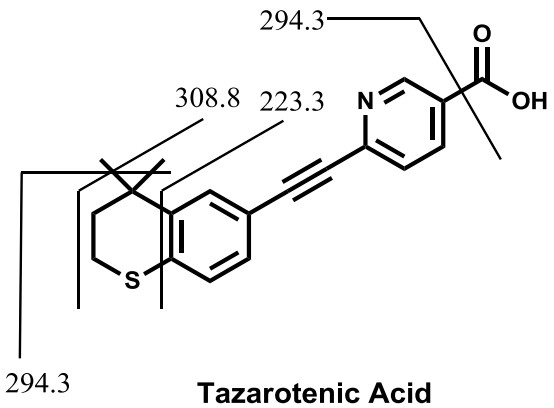
Supplemental Figure 3. Figure 6. Ligand interaction diagram for tazarotenic acid or tazarotenic acid sulfoxide docked in the active site of CYP26A1 and CYP26B1. Analysis of the active site ligand interactions for tazarotenic acid docked in the active site of CYP26A1 (A) and CYP26B1 (C) shows the hydrophobic (green), hydrophilic (blue), electrostatic (red/purple) and metal (pink) interactions located within 3.0 Å of tazarotenic acid. Ligand interactions for tazarotenic acid sulfoxide in the active site of CYP26A1 (B) and CYP26B1 (D) are also shown. Hydrogen bonding is depicted by dashed or solid lines.



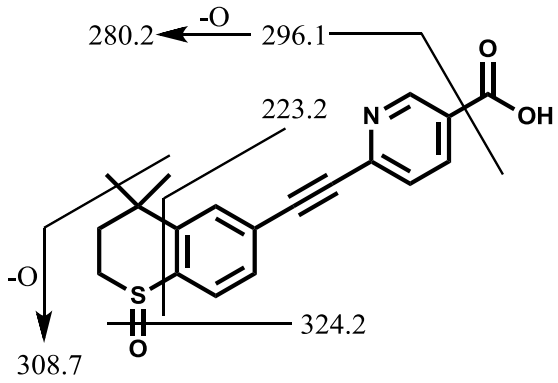
Supplemental Figure 4. MS-MS Spectrum For Tazarotenic Acid (m/z 324.2), Tazarotenic Acid Sulfoxide (m/z 340.3), Hydroxy-Tazarotenic Acid (m/z 340.3) and Tazarotenic Acid Sulfone (m/z 356.3)



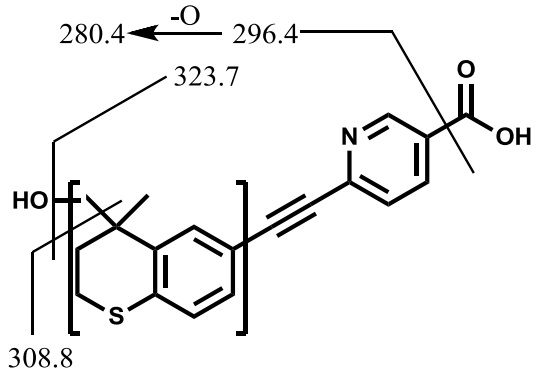
Supplemental Figure 5. Corresponding Fragmentation Pattern For Tazarotenic Acid (m/z 324.2), Tazarotenic Acid Sulfoxide (m/z 340.3), Hydroxy-Tazarotenic Acid (m/z 340.3) and Tazarotenic Acid Sulfone (m/z 356.3)



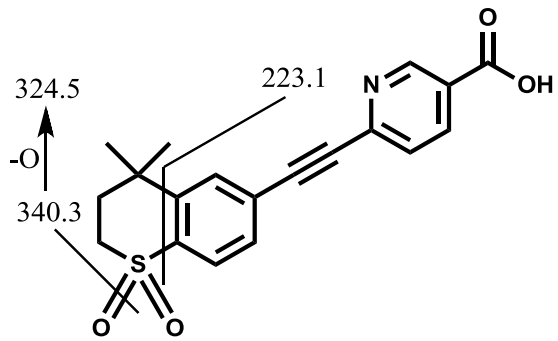
Tazarotenic Acid



Tazarotenic Acid Sulfoxide



Hydroxytazarotenic Acid



Tazarotenic Acid Sulfone